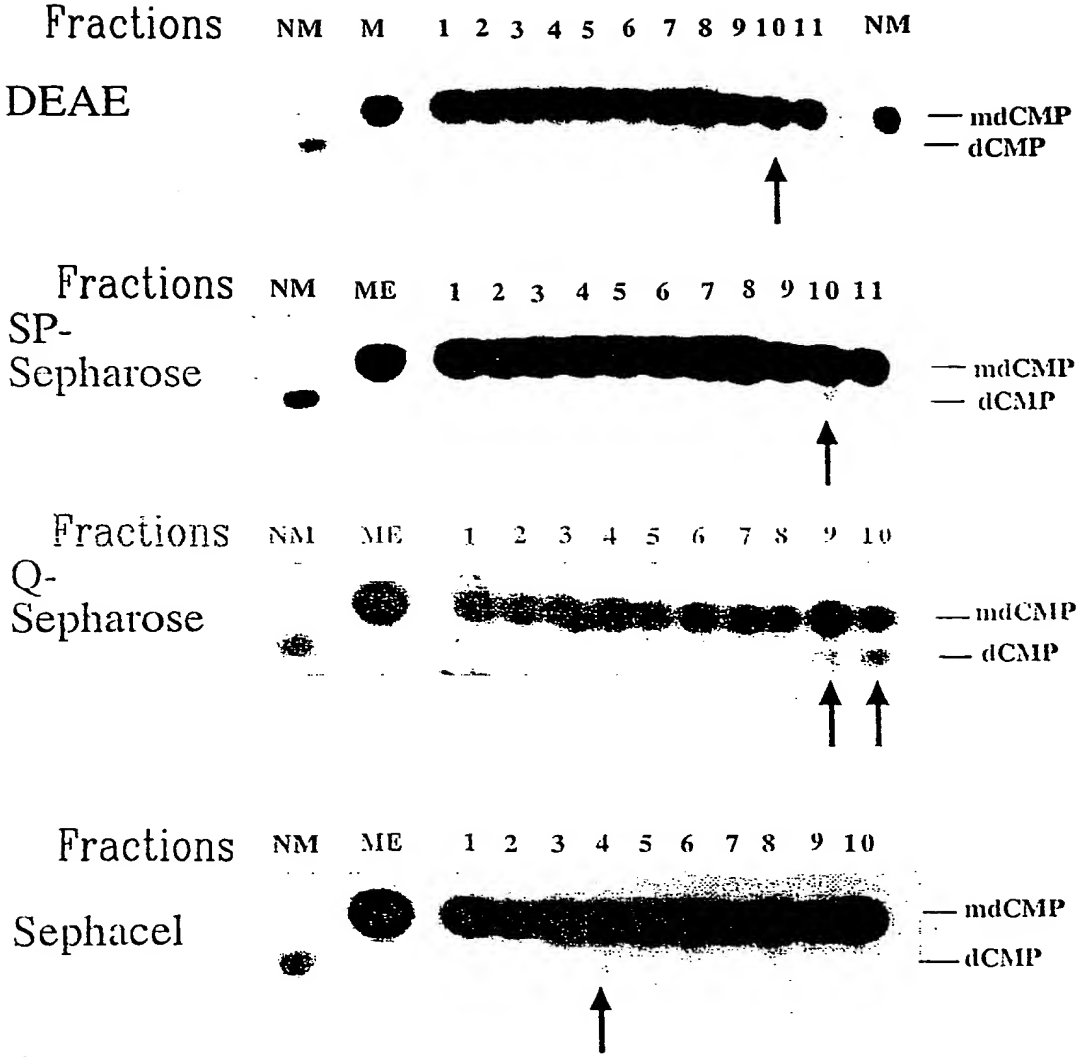


Fig. 1A

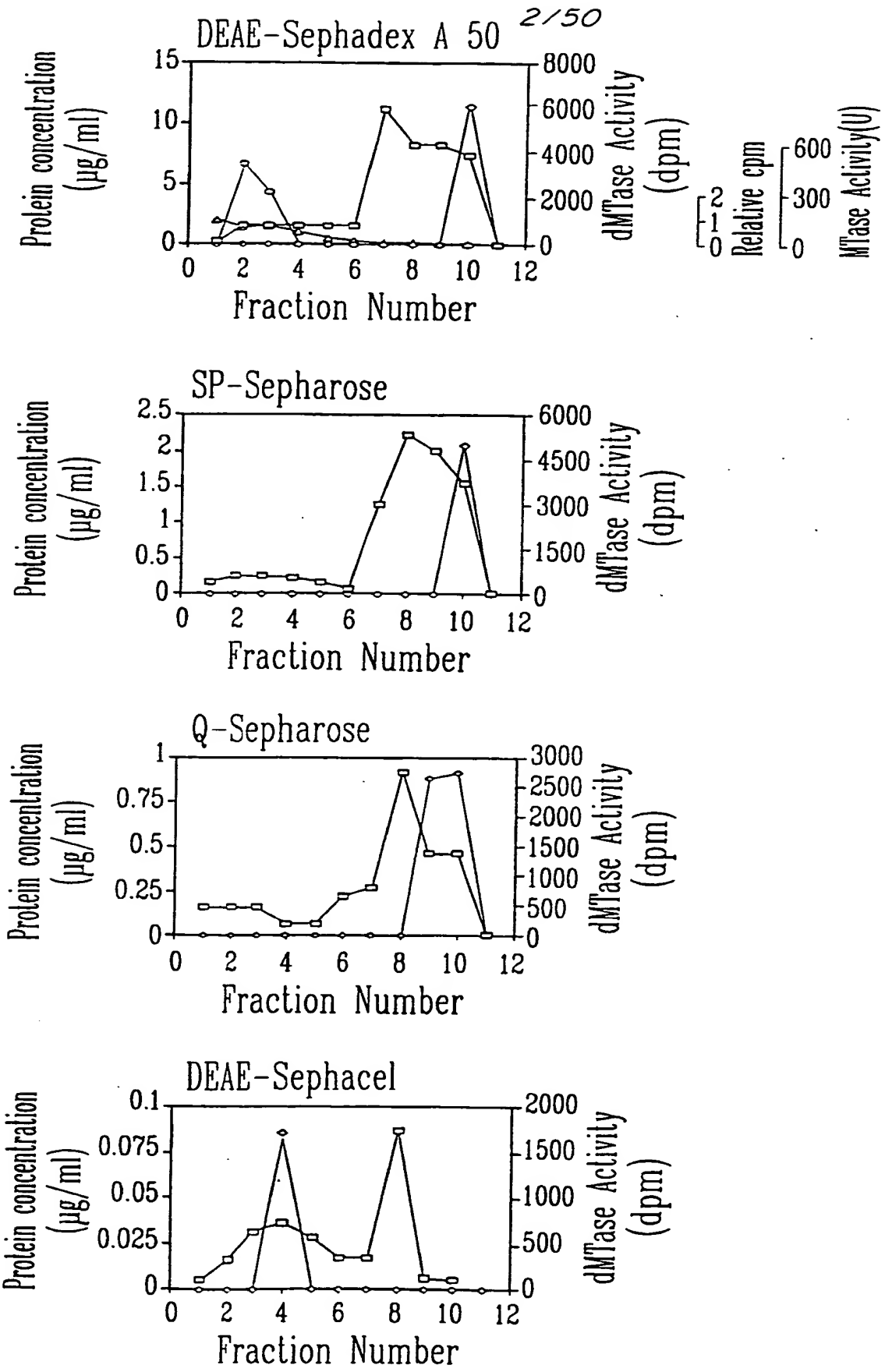

DEAE-Sephadex A 50
2/50
Protein concentration (µg/ml)
dMTase Activity (dpm)
Relative cpm
MTase Activity(U)
Fraction Number
SP-Sepharose
Protein concentration (µg/ml)
dMTase Activity (dpm)
Fraction Number
Q-Sepharose
Protein concentration (µg/ml)
dMTase Activity (dpm)
Fraction Number
DEAE-Sephacel
Protein concentration (µg/ml)
dMTase Activity (dpm)
Fraction Number

Fig. 1B

NM
ME
30 min
45 min
1 h
2 h
3 h
24 h
—dCMP
—mdCMP
Fig. 2B
NM
ME
DEAE-Sephadex
S-Sepharose
Q-Sepharose
Sephacel
ddCTP
mdCTP
-RNase
Proteinase K
—dCMP
—mdCMP
Fig. 2A

picomole cytosine formed
1.5
1.0
0.5
0
200
150
100
50
0
Time (min.)
Volatile Assay
CpG Assay
Methyl residues removed (dpm)
4000
3000
2000
1000
0

Fig. 2D

Methyl residues removed (dpm)
5000
4000
2000
1000
0
dMTase - + + -
ProteinaseK - + - -
RNase + + - +

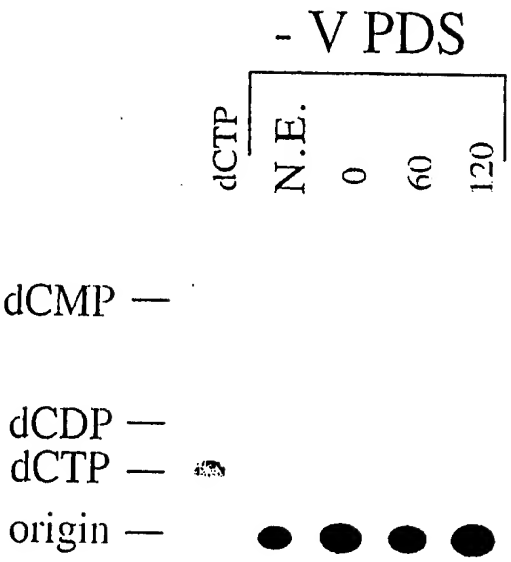
Fig. 2C

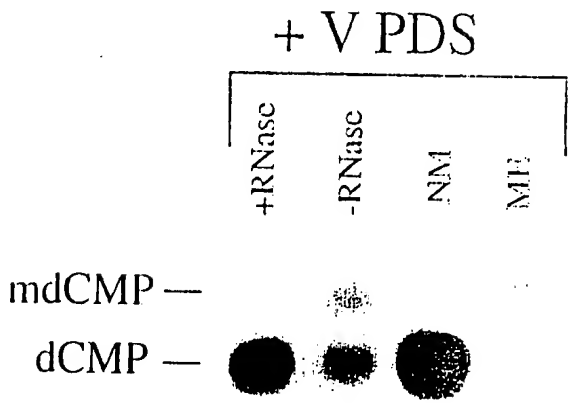
Fig - 3A

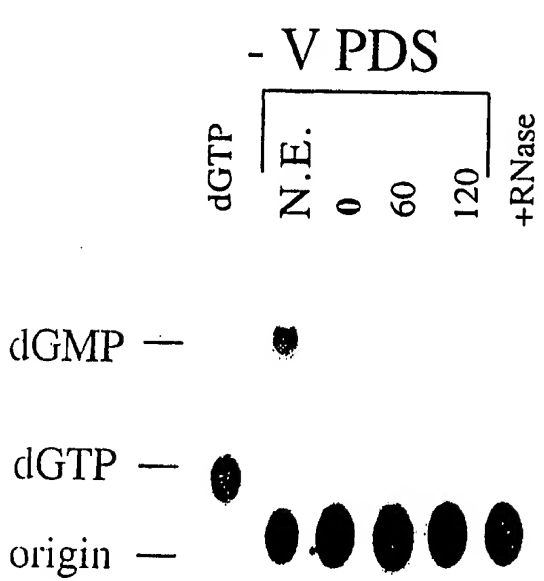
mdCMP
dCMP
NM
ME
+ dMTase
+dMTase + M. Sss1

Fig - 3B

meC
C
NM
ME
+ dMTase
+dMTase + M. Sss1
1st
2nd







Labeled nucleotide:
[α32P]-dCTP

Labeled nucleotide:
[α32P]-dGTP

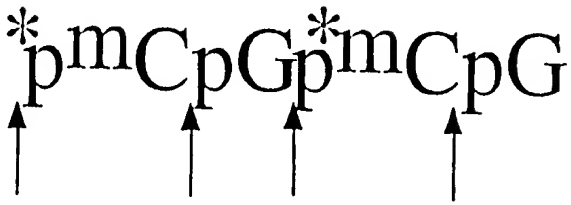


FIG. 3C

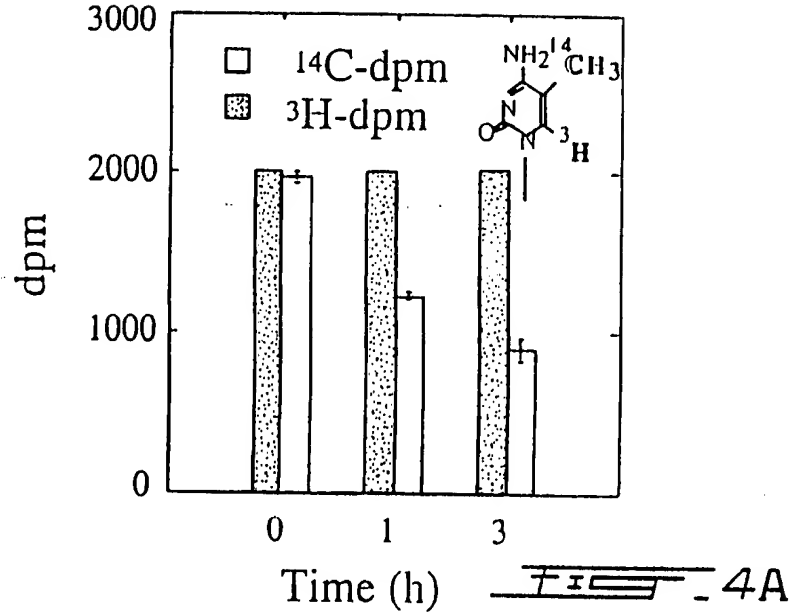
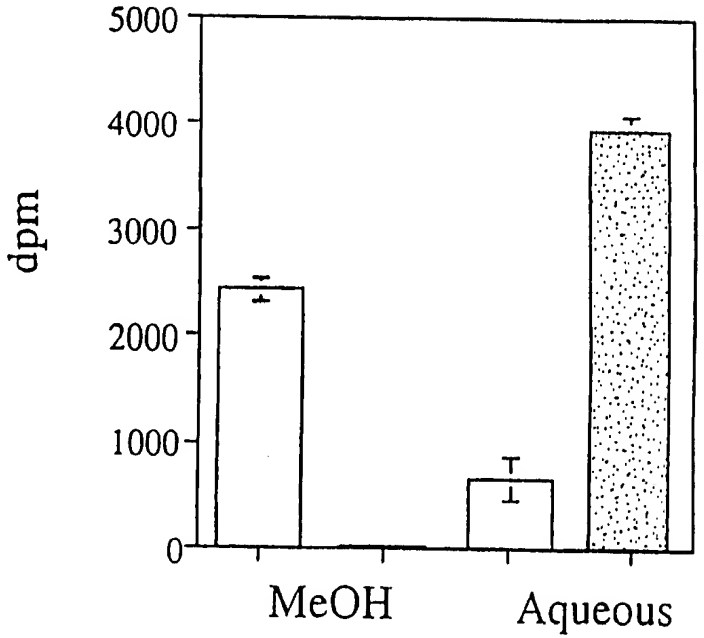


Fig 4A



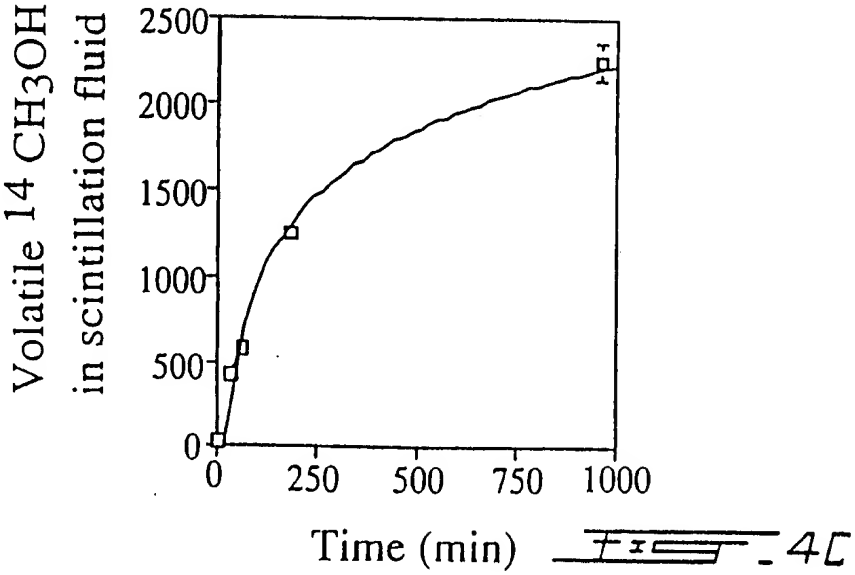


Fig 4C

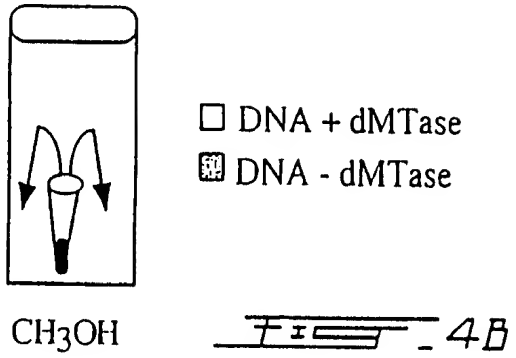


Fig 4B

dAMP
mdCMP
dCMP
dTMP
dGMP
methylated
15
30
60
120
180
Nonmethylated
15
30
60
120
180
dMT ase

Fig. 4D

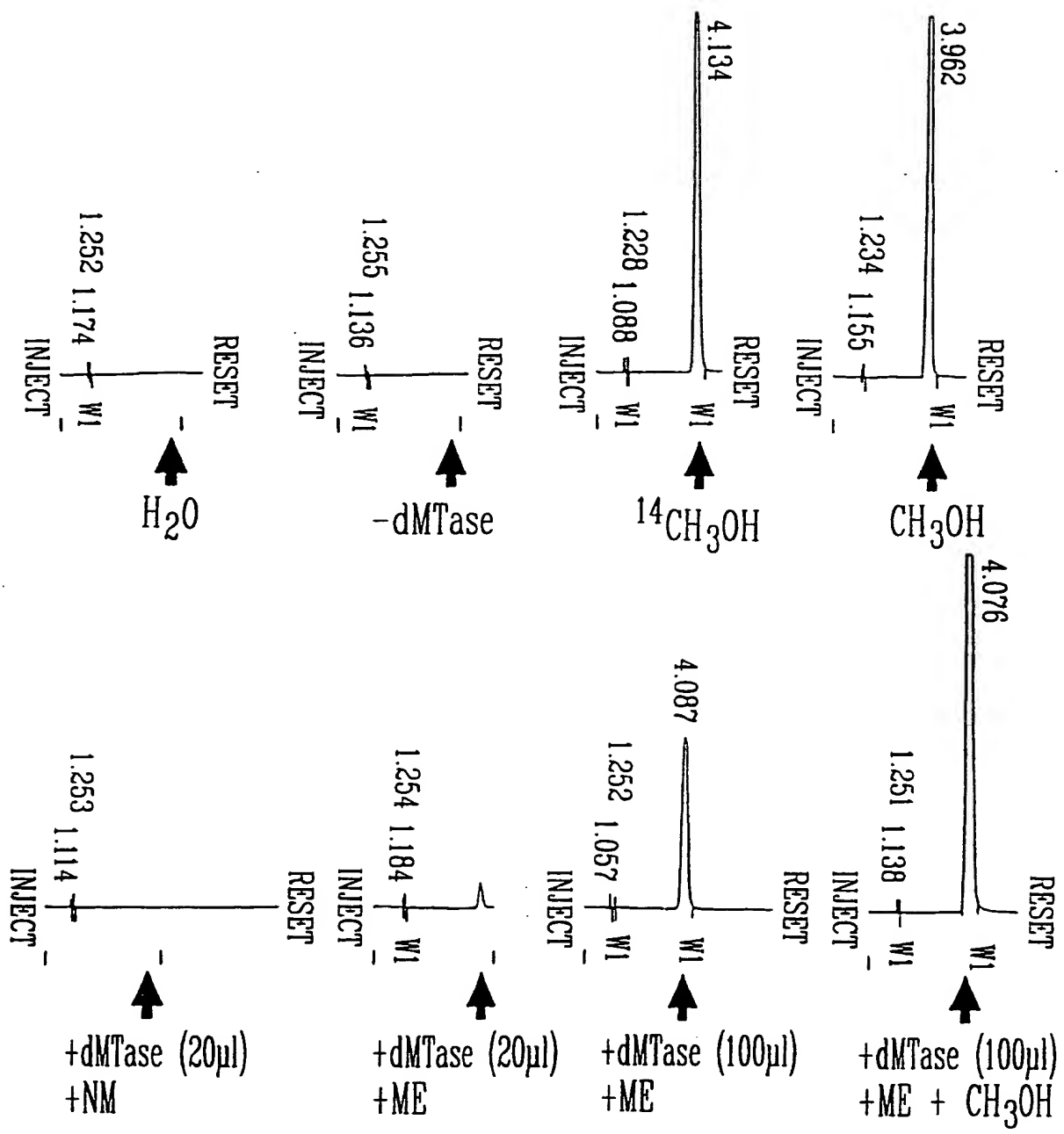

3.962
1.234
1.155
INJECT
W1
RESET
CH3OH
4.134
1.228
1.088
INJECT
W1
RESET
14CH3OH
1.255
1.136
INJECT
W1
RESET
-dMTase
1.252
1.174
INJECT
W1
RESET
H2O
4.076
1.251
1.138
INJECT
W1
RESET
+dMTase (100µl)
+ME + CH3OH
4.087
1.252
1.057
INJECT
W1
RESET
+dMTase (100µl)
+ME
1.254
1.184
INJECT
W1
RESET
+dMTase (20µl)
+ME
1.253
1.114
INJECT
RESET
+dMTase (20µl)
+NM

FIG 4E

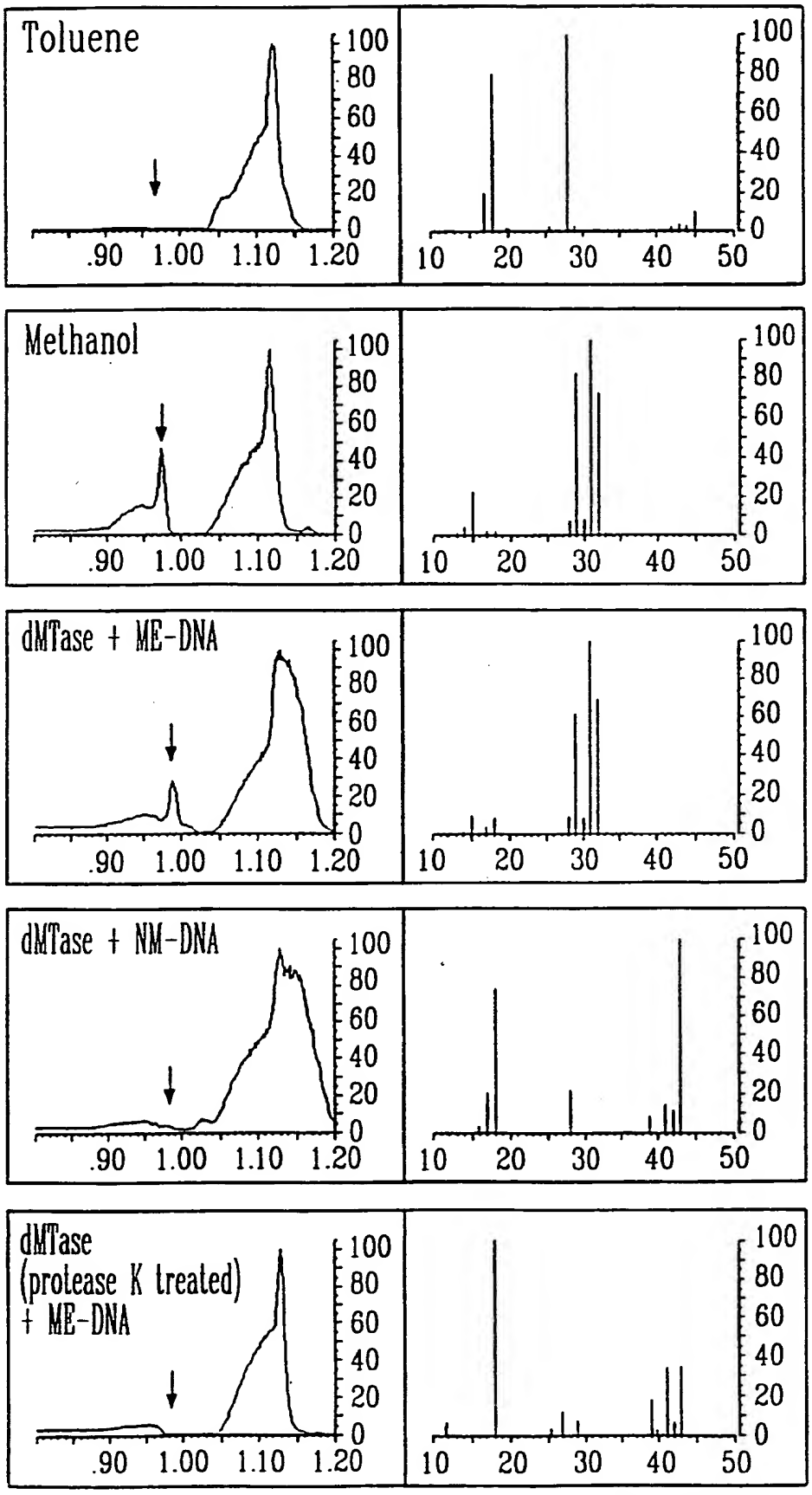
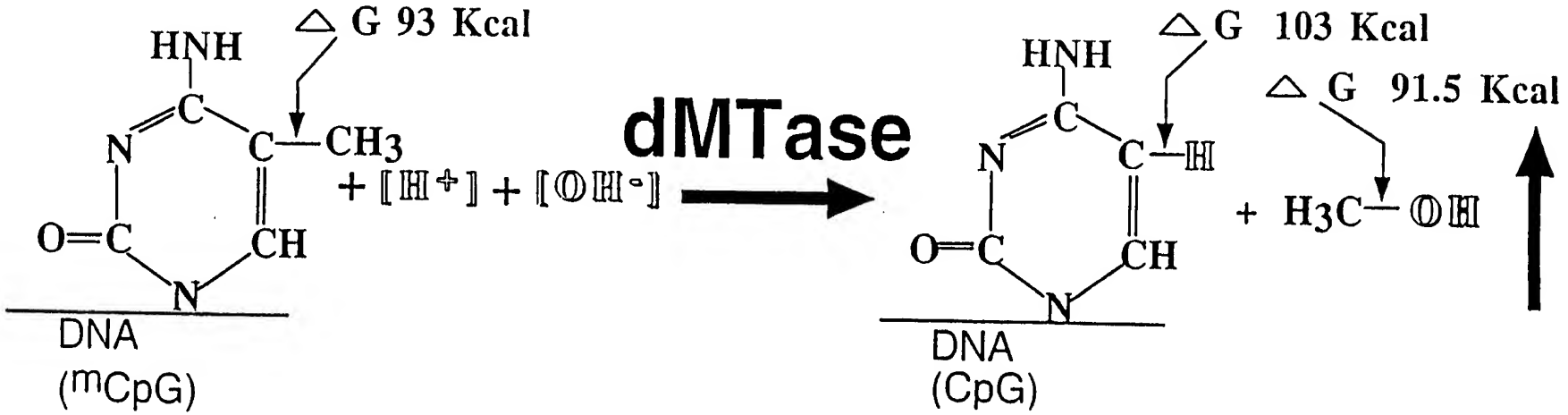

Toluene
Methanol
dMTase + ME-DNA
dMTase + NM-DNA
dMTase
(protease K treated)
+ ME-DNA
100
80
60
40
20
0
.90 1.00 1.10 1.20
10 20 30 40 50

Fig 4F



$$\triangle G_{Reaction} = (93) - (103 + 91.5) = (-101.5)\ Kcal$$

Fig. 5

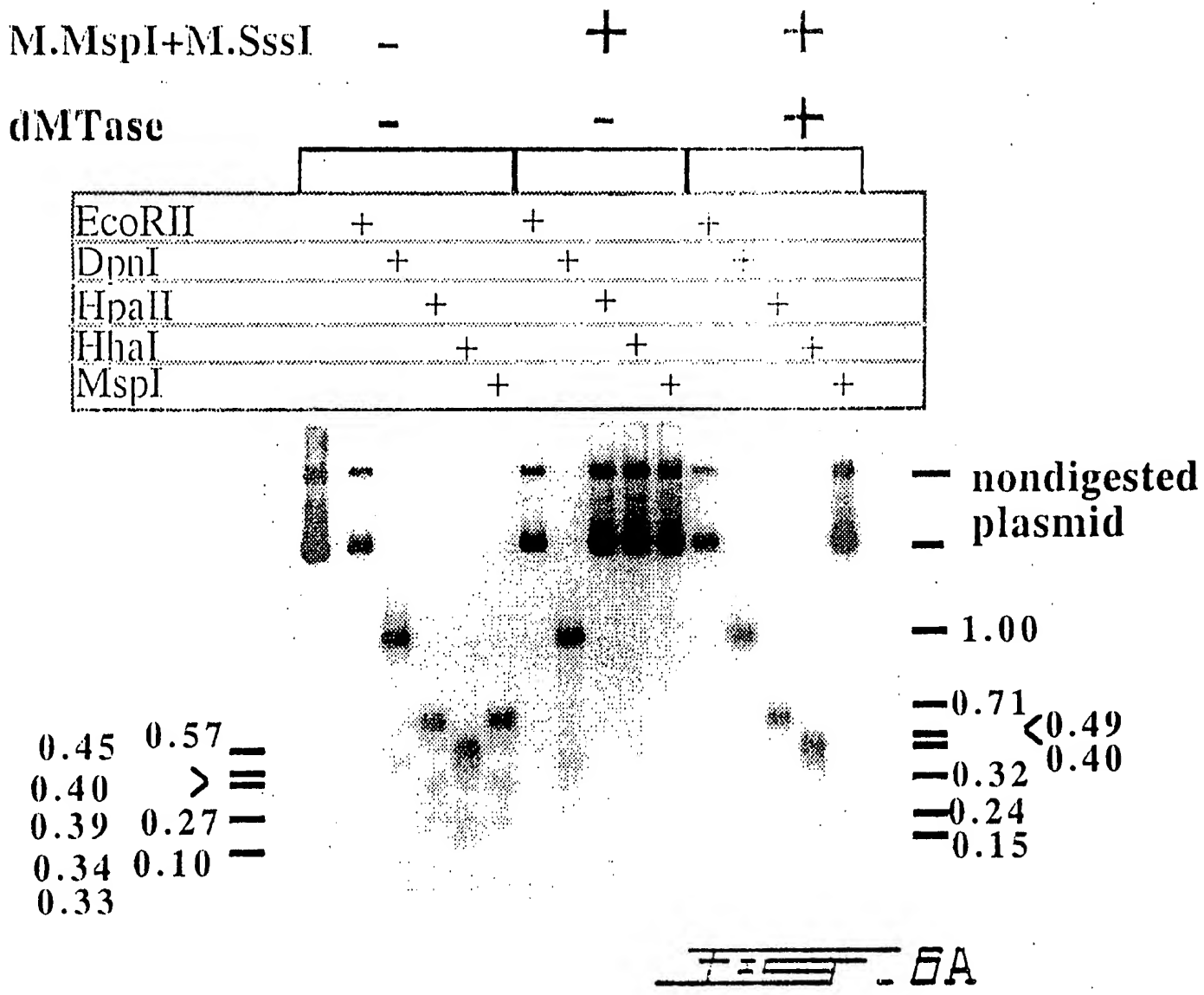


FIG. 6A

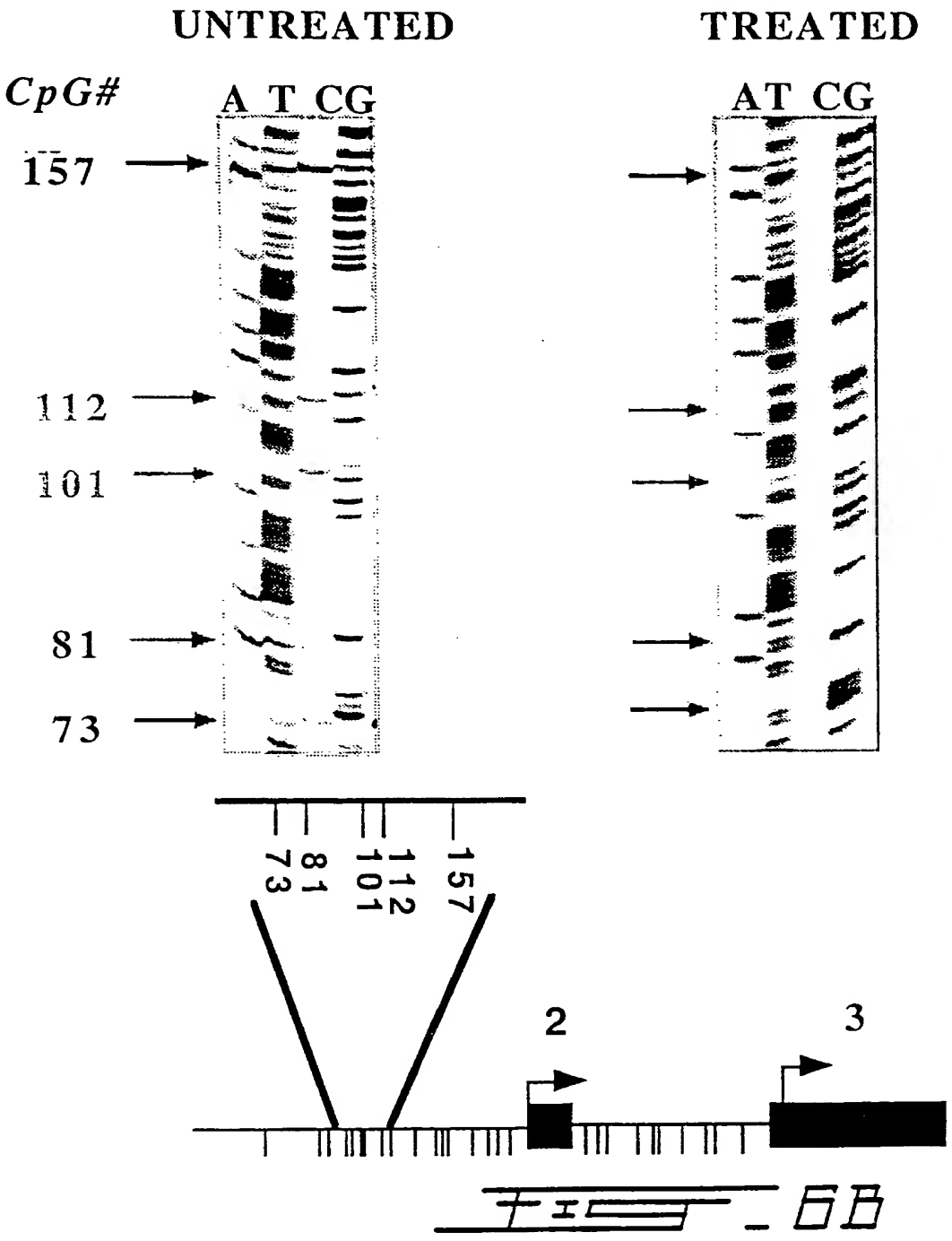


FIG 6B

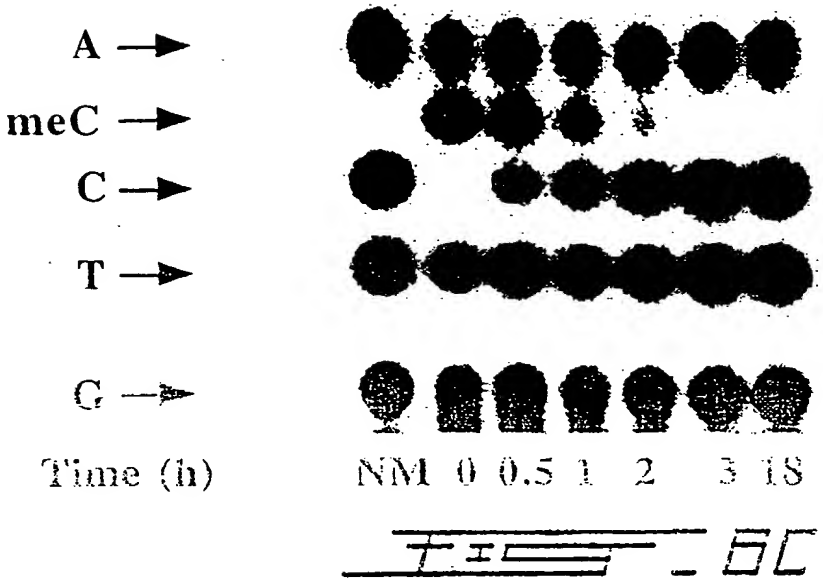

A
meC
C
T
G
Time (h)
NM 0 0.5 1 2 3 18

FIG 6C

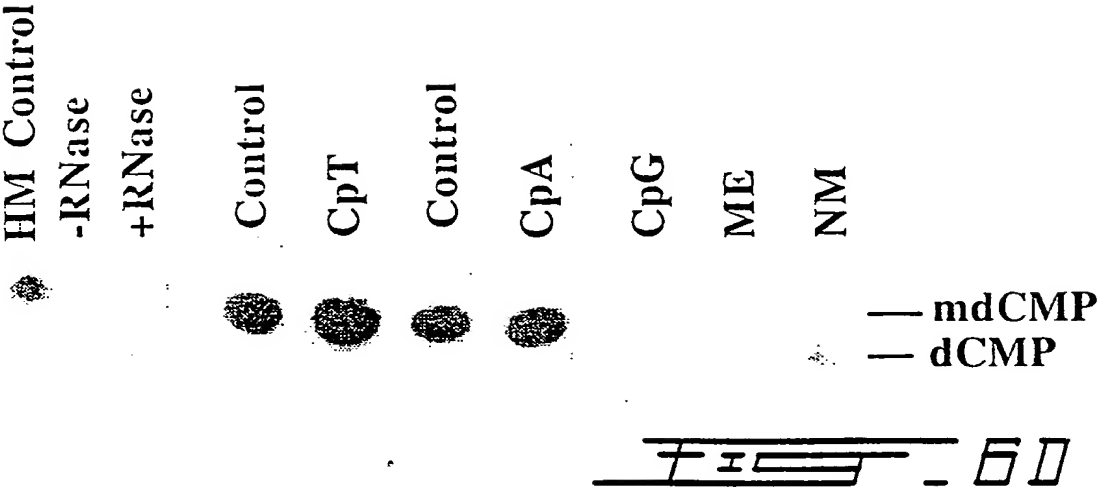

HM Control
-RNase
+RNase
Control
CpT
Control
CpA
CpG
ME
NM
mdCMP
dCMP

FIG 6D

FIG - 7B
200
Complex 150
MW (kDa)
200
116
97
66
44
32.5
column fraction
61 62 63 64 65
mdCMP
dCMP
CELL
DEAE
FIG - 7A
200
116
97
66
44
32.5
21.5

FIG - 7C

FIG - 7D

```
EST          DCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNIVDLS
             | | || ||     |||| |||| |||   | || |||| |  |    | |
             D P LP GW ++  RKSG SAGK DVY +P GK FRSK +L  Y    D S
             | | || ||     |||| |||| |||   | || |||| |  |    | |
MeCP2  15    DDPTLPEGWTRKLKQRKSGRSAGKYDVYLINPQGKAFRSKVELIAYFEKVGDTS 68
```

FIG. 8A

```
MDCPALPPGW KKEEVIRKSG LSAGKSDVYY FSPSGKKFRS  40
KPQLARYLGN TVDLSSFDFR TGKMMPSKLQ KNKQRLRNDP  80
LNQNKGKPDL NTTLPIRQTA SIFKQPVTKV TNHPSNKVKS 120
DPQRMNEQPR QLFWEKRLQG LSASDVTEQI IKTMELPKGL 160
QGVGPGSNDE TLLSAVASAL HTSSAPITGQ VSAAVEKNPA 200
VWLNTSQPLC KAFIVTDEDI RKQEERVQQV RKILEDALMA 240
DILSRAADTE EMDIEMDSGD EA                    262
```

(wavy underline) homology to methylated DNA binding domain

(hatched bar) homology to coiled coil domain

FIG. 8B

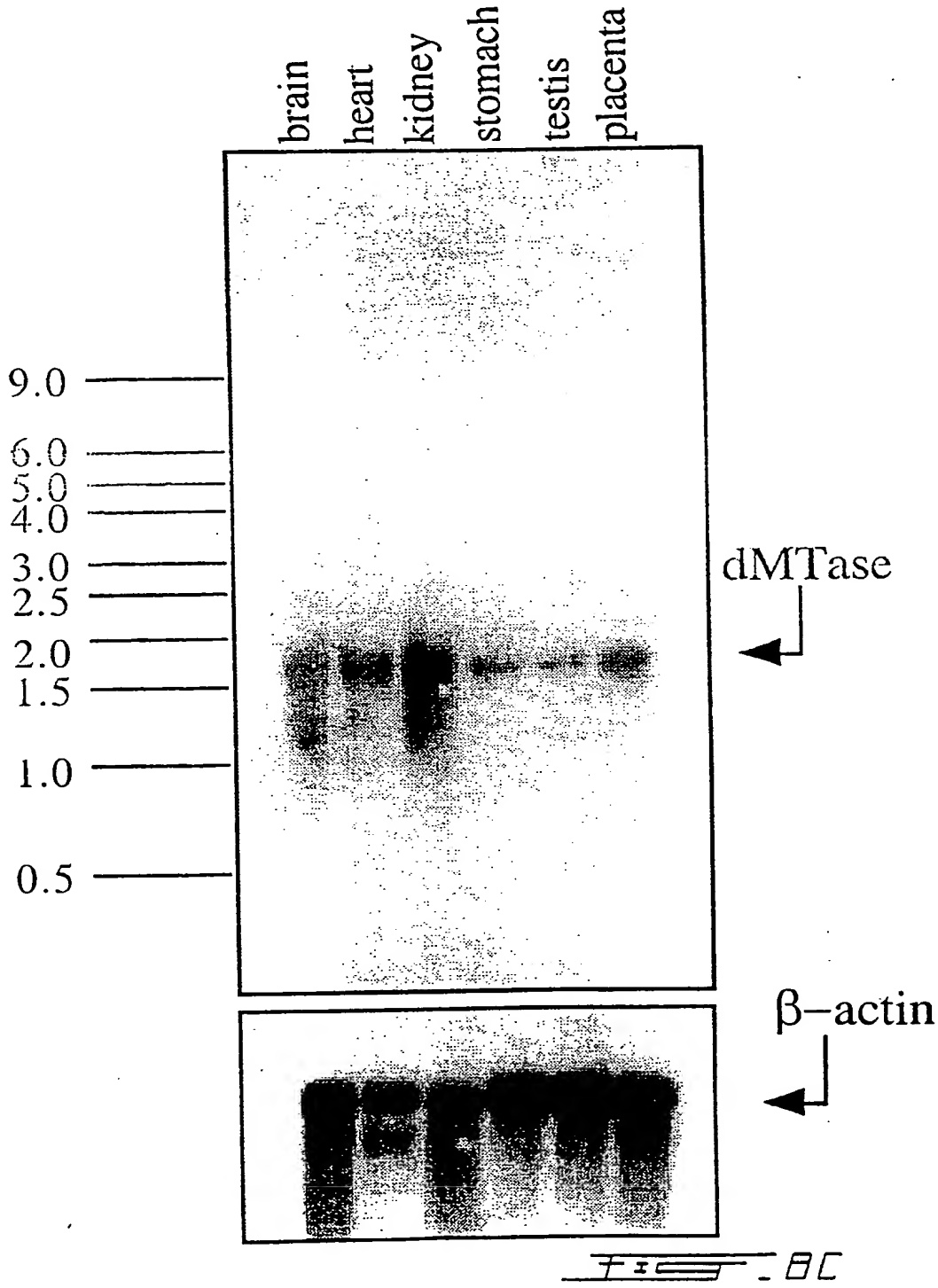

brain
heart
kidney
stomach
testis
placenta
9.0
6.0
5.0
4.0
3.0
2.5
2.0
1.5
1.0
0.5
dMTase
β–actin

Fig. 8C

Human DNA demethylase cDNA-dMTase1 and predicted amino acid sequence

```
5'ggggggcgtgg ccccgagaag gcggagacaa gatggccgcc catagcgctt ggaggaccta
 agaggcggtg gccgggggcca cgccccgggc aggagggccg ctctgtgcgc gcccgctcta
 tgatgcttgc gcgcgtcccc cgcgcgcccgc gctgcgggcg gggcgggtct ccgggattcc
 aagggctcgg ttacggaaga agcgcagcgc cggctgggga ggggggctgga tgcgcgcgca
 cccgggggga ggccggctgct gcccggagca ggaggagggg gagagtgcgg cgggcggcag
 cggcgctggc ggcgactccg ccatagagca ggggggccag ggcagcgcgc tcgccccgtc
 ccggcgtgagc ggcgtgcgca gggaaggcgc tcgggggcggc ggccgtgggc ggggggcggtg
 gaagcaggcg ggccgggggcg gcggcgtctg tggccgtggc cgggggccggg gccgtggccg
 gggacgggga cgggggccggg gccgggggccg cggccgtccc ccgagtgggcg gcagcggcct
 tggcggcgac ggcggcggct gcggcgcggg cggcagcggt ggcggcgcgg ccccccggcg
 ggagccggtc cctttcccgt cgggggagcgc ggggccgggg cccagggggac cccgggccac
 ggagagcggg aagaggatgg attgcccggc cctccccccc ggatgggaaga aggaggaagt
 gatccgaaaa tctgggctaa gtgctgggcaa gagcgatgtc tactacttca gtccaagtgg
 taagaagttc agaagcaagc ctcagttggc aaggtacctg ggaaatactg ttgatctcag
 cagtttgac ttcagaactg gaaagatgat gcctagtaaa ttacagaaga acaaacagag
 actgcgaaac gatcctctca atcaaaataa gggtaaacca gacttgaata caacattgcc
 aattagacaa acagcatcaa tttcaaaaca accggtaacc aaagtcacaa atcatcctag
```

FIG - 9A

taataaagtg aaatcagacc cacaacgaat gaatgaacag ccacgtcagc ttttctggga
gaagaggcta caaggactta gtgcatcaga tgtaacagaa caaattataa aaaccatgga
actacccaaa ggtcttcaag gagttggtcc aggtagcaat gatgagaccc ttttatctgc
tgttgccagt gctttgcaca caagctctgc gccaatcaca gggcaagtct ccgctgctgt
ggaaaagaac cctgctgttt ggcttaacac atctcaaccc ctctgcaaag cttttattgt
cacagatgaa gacatcagga aacaggaaga gcgagtacag caagtacgca agaaattgga
agaagcactg atggcagaca tcttgtcgcg agctgctgat acagaagaga tggatattga
aatggacagt ggagatgaag cctaagaata tgatcaggta actttcgacc gactttcccc
aagrgaaaat tcctagaaat tgaacaaaaa tgtttccact ggcttttgcc tgtaagaaaa
aaaatgtacc cgagcacata gagcttttta atagcactaa ccaatgcctt tttagatgta
tttttgatgt atatatctat tattcaaaaa atcatgttta ttttgagtcc taggacttaa
aattagtctt ttgtaatatc aagcaggacc ctaagatgaa gctgagcttt tgatgccagg
tgcaatctac tggaaatgta gcacttacgt aaaacatttg tttcccccac agttttaata
agaacagatc aggaattcta aataaatttc ccagttaaag attattgtga cttcactgta
tataaacata tttttatact ttattgaaag gggacacctg tacattcttc catcatcact
gtaaagacaa ataaatgatt atattcacaa aaaaaaaaaa aaaaaa 3'

SEQ ID NO:1

Fig 9B

MRAHPGGGRCCPEQEEGESAAGGSGAGGDSAIEQGGQGSALAPSPVSGVR
REGARGGGRGRGRWKQAGRGGGVCGRGRGRGRGRGRGRGRGRGRPPSG
GSGLGGDGGGCGGGGSGGGGAPRREPVPFPSGSAGPGPRGPRATESGKRM
DCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNT
VDLSSFDFRTGKMMPSKLQKNKQRLRNDPLNQNKGKPDLNTTLPIRQTAS
IFKQPVTKVTNHPSNKVKSDPQRMNEQPRQLFWEKRLQGLSASDVTEQII
KTMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAV
WLNTSQPLCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAADTEE
MDIEMDSGDEA

SEQ ID NO:2

Fig 9C

Human DNA demethylase homologue-dMTase2 and predicted amino acid sequence

```
5'agcgggccga ggagccgggc gcaatggagc ggaagaggtg ggagtgcccg gcgctcccgc
  agggctggga gagggaagaa gtgcccagaa ggtcggggct gtcggccggc cacagggatg
  tcttttacta tagcccgagc gggaagaagt tccgcagcaa gccgcagctg gcgcgctacc
  tgggcggctc catggacctg agcaccttcg acttccgcac gggcaagatg ctgatgagca
  agatgaacaa gagccgccag cgcgtgcgct acgactcctc caaccaggtc aagggcaagc
  ccgacctgaa cacggcgctg cccgtgcgcc agacggcgtc catcttcaag cagccggtga
  ccaagattac caaccacccc agcaacaagg tcaagagcga cccgcagaag gcggtggacc
  agccgcgcca gctcttctgg gagaagaagc tgagcggcct gaacgccttc gacattgctg
  aggagctggt caagaccatg gacctcccca agggcctgca gggggtggga cctggctgca
  cggatgagac gctgctgtcg gccatcgcca gcgccctgca cactagcacc atgcccatca
  cgggacagct ctcggccgcc gtggagaaga accccggcgt atggctcaac accacgcagc
  ccctgtgcaa agccttcatg gtgaccgacg aggacatcag gaagcaggaa gagctggtgc
  agcaggtgcg gaagcggctg gaggaggcgc tgatggccga catgctggcg cacgtggagg
  agctggcccg tgacggggag gcgccgctgg acaaggcctg cgctgaggac gacgacgagg
  aagacgagga ggaggaggag gaggagcccg acccggaccc ggagatggag cacgtctagg
  gcagaggccc tgccgagagc ccgtgctgcc tgctggagcc gcctgcagac gcggtcctcg
  gccccacgtg aaccaggctc ggcggcgaag cccagccttg gagacaccca ggaggaaggc
  cgtgctcctg gctccctcct cggcccgtcc ccacttcccg gggcctcggg gcacacagct
  ggggctgccc ccacccgaaa gaccctccac gctcgtcctc tacagagtcc ggcttcggga
  agtgccgggt gctcctgggc cctgcctggc tccctacgac ctttgggctc gaggccagct
```

Fig. 9D

cctccccatg cccgctgtcc cagctccttg agactggaga gcagccagca ggtgcccggc
agctcggcgc cacggcttgc tgacagctgg gagggtttct cggtctggag gcgtagtttt
gaaactcaca tcacccactg tgcagcgtga ggacgggact ctggtctgct gtgggggca
tgcaggacgg cgccactctc tgccctgcca tgcggctggt ggtgccacag agcctcaccg
tgcctgagtg gcgtgcccag ggaggccgct ctccttcagt aaatgtaaca cagtcgaggc
acgtcatcgg gcagccttcc ctgtgtgcca acgccagcct tcgcttctga aaaccaaact
ccagccgctg ccagtcggga cttggtcgcc cggcgctgcc agaatgctcc actgccagcc
ggcccccctg cctcggtttc ccttctgttt agtggcgaca caggcaccca gctttggggt
ggtgctgacg ctcccagggg tgccaggagc cactgggaca gggtgaggct cccagacgct
cctcgaggtg cccagctctc cagggagctt ctggcccaag gcgttcttga gggatctgct
ccttaacccc ccagtgcctt ggcgagggca ggttccaagc cacagacgcc tgccccgagt
ggactttgcg gccagtccct gggtgccttc ctgggccctg cttgcccagt gagggttcct
aacgggtggg ttcawtggcc tggcccvagc gagcccccac ctgcattgac cttaggccca
tagagagggc ctgtcccggt gctgccccag ccaaggatct ggtcgctgcc ccaggggac
tgatgggcaa gagtcgcccc tgtggctgga ctgtgaccat ccctgatggg gcctgaccgc
gggagctgag gaagcgccgc tccaccgtct gccctccaag gacccgcatg gaggcagtgg
gctggcagct tcctgctgct ccctgtcaga gtcaaagcac aaatcctcag gacgggctca
agggccaggg cagccgaggg aagctccagg tggggaccac gtcttcctga ggttggtgcc
cactggctgg gaccctttgc agtggggtgg cctcccctct gtctgcctgg tggagggagc
cgtgggcgtg gggacgtgac tgaataaagc caccatgggt ggatgtgctt gg 3'

SEQ ID NO:3

FIG 9E

MERKRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLA
RYLGGSMDLSTFDFRTGKMLMSKMNKSRQRVRYDSSNQVKGKPDLNTALP
VRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKLSGLNAFD
IAEELVKTMDLPKGLQGVGPGCTDETLLSAIASALHTSTMPITGQLSAAV
EKNPGVWLNTTQPLCKAFMVTDEDIRKQEELVQQVRKRLEEALMADMLAH
VEELARDGEAPLDKACAEDDDEEDEEEEEEPDPDPEMEHV

SEQ ID NO:4

Fig. 9F

Lipman-Pearson Protein Alignment
Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12

Seq1(1>411)	Seq2(1>291)	Similarity	Gap	Gap	Consensus
human dMTase1 protein	human dMTase2 protein	Index	Number	Length	Length
(148>397)	(4>253)	76.0	0	0	250
(148>397)	(4>253)	76.0	0	0	250

```
  v150       v160       v170       v180       v190       v200       v210
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNIVDLSSFDFRTGKMMPSK
KR :CPALP.GW.:EEV R:SGLSAG..DV:Y:SPSGKKFRSKPQLARYLG.::DLS:FDFRTGKM: SK
KRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLARYLGGSMDLSTFDFRTGKMLMSK
      ^10        ^20        ^30        ^40        ^50        ^60        ^70

  v220       v230       v240       v250       v260       v270       v280
LQKNKQRLRNDPLNQNKGKPDLNTTLPIRQTASIFKQPVTKVTNHPSNKVKSDPQRMNEQPRQLFWEKRL
::K::QR:R D: NQ KGKPDLNT:LP:RQTASIFKQPVTK:TNHPSNKVKSDPQ:   :QPRQLFWEK:L
MNKSRQRVRYDSSNQVKGKPDLNTALPVRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKL
      ^80        ^90        ^100       ^110       ^120       ^130       ^140
```

FIG - 9G

```
  v290       v300       v310       v320       v330       v340       v350
QGLSASDVTEQIIKIMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAVWLNISQP
 GL:A D::E:::KIM:LPKGLQGVGPG..DETLLSA:ASALHTS: PITGQ:SAAVEKNP:VWLNT:QP
SGLNAFDIAEELVKIMDLPKGLQGVGPGCTDETLLSAIASALHTSTMPITGQLSAAVEKNPGVWLNITQP
      ^150       ^160       ^170       ^180       ^190       ^200       ^210

  v360       v370       v380       v390
LCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
LCKAF:VTDEDIRKQEE VQQVRK:LEEALMAD:L::..:
LCKAFMVTDEDIRKQEELVQQVRKRLEEALMADMLAHVEE
      ^220       ^230       ^240       ^250
```

Fig 9H

Mouse DNA demethylase-dMTase1 and predicted amino acid sequence

```
5'ccgctctgcg ggcggggcgg gtctccggga ttccaagggc tcggttacgg aagaagcgca
  gagccggctg gggagggggc tggatgcgcg cgcacccggg gggaggccgc tgctgcccgg
  agcaggagga gggggagagc gcggcgggcg gcagcggcgc tggcggcgac tccgccatag
  agcaggggggg ccagggcagc gcgctcgctc cgtccccggt gagcggcgtg cgcagggaag
  gcgctcgggg cggcggccgt ggccgggggc ggtggaagca ggcggcccgg ggcggcggcg
  tctgtggccg tggccgtggc cgtggccggg gtcggggccg tggccggggc cggggccggg
  gccgcggccg tccccagagt ggcggcagcg gccttggcgg cgacggcggc ggcggcgcgg
  gcggctgcgg cgtcggcagc ggtggcggcg tcgccccccg gcgggatcct gtccctttcc
  cgtcggggag ctcggggccg gggcccaggg gaccccgggc cacggagagc gggaagagga
  tggactgccc ggccctcccc cccggatgga agaaggagga agtgatccga aaatcagggc
  tcagtgctgg caagagcgat gtctactact tcagtccaag tggtaagaag ttcagaagta
  aacctcagct ggcaagatac ctgggaaatg ctgttgacct tagcagtttt gacttcagga
  ccggcaagat gatgcctagt aaattacaga agaacaagca gagactccgg aatgaccccc
  tcaatcagaa caagggtaaa ccagacctga acacaacatt gccaattaga caaactgcat
  caattttcaa gcaaccagta accaaattca cgaaccaccc gagcaataag gtgaagtcag
  acccccagcg gatgaatgaa caaccacgtc agcttttctg ggagaagagg ctacaaggac
  ttagcgcatc agatgtaaca gaacaaatta taaaaaccat ggagctacct aaaggtcttc
  aaggagtcgg tccaggtagc aatgacgaga cccttctgtc tgctgtggcc agtgctttac
```

FIG - 91

27/50

acacaagctc tgcgcccatc acaggacaag tctctgctgc cgtggaaaag aaccctgctg
tttggcttaa cacatctcaa cccctctgca aagctttcat tgttacagat gaagacatta
ggaaacagga agagcgagtc caacaagtac gcaagaaact ggaggaggca ctgatggccg
acatcctgtc ccgggctgcg gacacggagg aagtagacat tgacatggac agtggagatg
aggcgtaaga atatgatcag gtaactttcg actgaccttc cccaagagca aattgctaga
aacagaatta aaacatttcc actgggtttc gcctgtaaga aaaagtgtac ctgagcacat
agcttttaa tagcactaac caatgccttt ttagatgtat ttttgatgta tatatctatt
attccaaatg atgtttattt tgaatcctag gacttaaaat gagtctttta taatagcaag
cagggccctt ccggtgcagt gcagctttga ggccaggtgc agtctactgg aaaggtagca
cttacgtgaa atatttgttt cccccacagt tttaatataa acagatcagg agtaccaaat
aagtttccca attaaagatt attatacttc actgtatata aacagatttt tatactttat
tgaaagaaga tacctgtaca ttcttccatc atcactgtaa agacaaataa atgactatat
tcac 3′

SEQ ID NO:5

FIG. 9J

MRAHPGGGRCCPEQEEGESAAGGSGAGGDSAIEQGGQGSALAPSPVSGVR
REGARGGGRGRGRWKQAARGGGVCGRGRGRGRGRGRGRGRGRGRPQSG
GSGLGGDGGGGAGGCGVGSGGGVAPRRDPVPFPSGSSGPGPRGPRATESG
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYL
GNAVDLSSFDFRTGKMMPSKLQKNKQRLRNDPLNQNKGKPDLNTTLPIRQ
TASIFKQPVTKFTNHPSNKVKSDPQRMNEQPRQLFWEKRLQGLSASDVTE
QIIKTMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKN
PAVWLNTSQPLCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
TEEVDIDMDSGDEA

SEQ ID NO:6

Fig 9K

Mouse DNA demethylase-dMTase2 and predicted amino acid sequence

```
5'cacgcgcggg cgggtgggcg gagcggcccc cctagcgggg gctgtgaagc gcggggaggg
  ggccgagcgg gtggcgaagc cggcgcgcgc ccggctgggg gcggagggcg gaggcccgtg
  ggacagaaca gctgcggcga gtggcggcgg cggagggagc cgaatcggcg acgagcccgg
  gggtcgcaac ttgcagaagc ggcggcggcg gcggcatcgg ccacggcggg cggaaaagcc
  ggggcgcaat ggagcggaag aggtgggagt gcccggcgct cccgcagggc tgggaaaggg
  aagaagtgcc caggaggtcg gggctgtcgg ccggccacag ggatgtcttt tactatagcc
  ccagcgggaa gaagttccgc agcaagccac aactggcacg ttacctgggc ggatccatgg
  acctcagcac cttcgacttc cgcaccggaa agatgttgat gaacaagatg aataagagtc
  gccagcgtgt gcgctatgat tcttccaacc aggtcaaggg caagcctgac ctgaacaccg
  cgctgcctgt acggcagact gcatccatct tcaagcaacc ggtgaccaag atcaccaacc
  accccagcaa caaggtcaag agcgacccgc agaaggcagt ggaccagccg aggcagcttt
  tctgggagaa gaagctaagt ggattgagtg cctttgacat tgcagaagaa ctggtcagga
  ccatggactt gcccaagggc ctgcagggag tgggccctgg ctgtacagat gagacgctgc
  tgtcagccat tgcgagtgct ctacacacca gcaccctgcc cattacaggc cagctctctg
  cagccgtgga gaagaaccct ggtgtgtggc tgaacactgc acagccactg tgcaaagcct
  tcatggtgac agatgacgac atcaggaagc aggaggagct ggtacagcag gtacggaagc
  gcctggagga ggcactgatg gccgacatgc tagctcatgt ggaggagctt gcccgagacg
  gggaggcacc actggacaag gcctgtgcag aggaggaaga ggaggaggaa gaggaggagg
```

FIG. 7G

aagagccgga gccagagcga gtgtagcaca ggtgccctgc ccaagtctgg gctgcagact
gccttcagcc ttgcctggac caggtagggg ccagacctgt aggaggcagc cgtccacctc
ctttccaaag cctcctgctt ccaggtctca gtgcagggag cccctgtgga ccttgaactc
acttgtccct gcgctgcctg gcaggaagcc ccacactgaa agcagatgag cagtgaccca
actgagaggc cacctggaca cagtcacctc cctgcctcct tatcatagga caaggccttg
cttggcaccg aggagctggg agccgtgttg ggtgctggag gaagtttctg gaaacacacc
tggctatgcc caccttatgt ccctaaggct attacaggcc agggtttgga ctgctccggc
ccacagggct gcccagcctc cccacactga gggtcagcag cccaccagga agtcactttc
cttcaataaa ctgatggtag gaacttgtg 3'

SEQ ID NO:7

FIG. 9M

MERKRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLA
RYLGGSMDLSTFDFRTGKMLMNKMNKSRQRVRYDSSNQVKGKPDLNTALP
VRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKLSGLSAFD
IAEELVRTMDLPKGLQGVGPGCTDETLLSAIASALHTSTLPITGQLSAAV
EKNPGVWLNTAQPLCKAFMVTDDDIRKQEELVQQVRKRLEEALMADMLAH
VEELARDGEAPLDKACAEEEEEEEEEEEPEPERV

SEQ ID NO:8

FIG. 9N

PCT/CA98/01059

Lipman-Pearson Protein Alignment
Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12

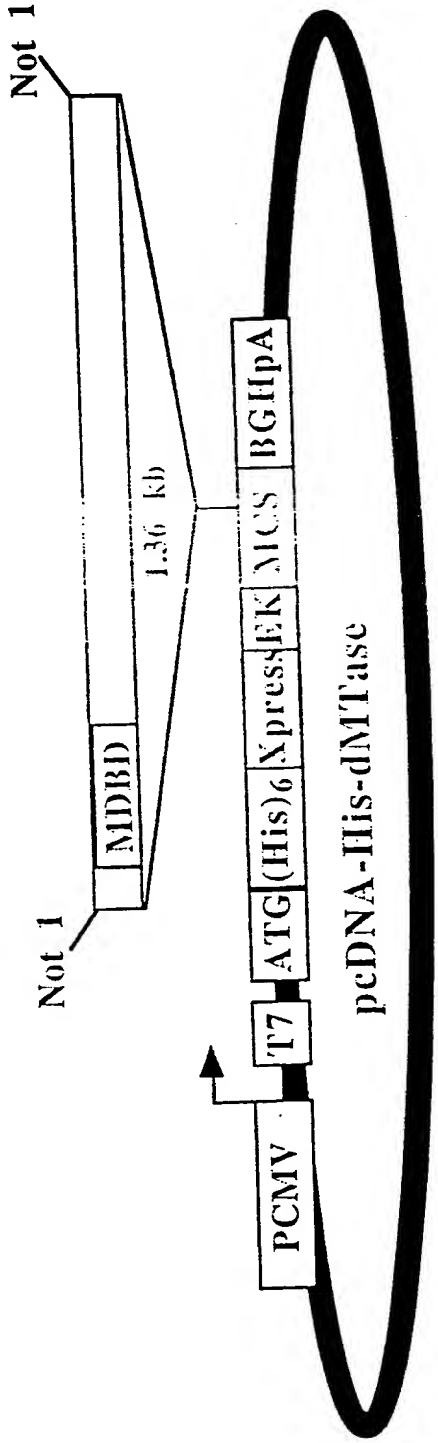
Seq1(1>414)	Seq2(1>285)	Similarity	Gap	Gap	Consensus
mouse dMTase1 protein	mouse dMTase2 protein	Index	Number	Length	Length
(151>400)	(4>253)	75.2	0	0	250
(151>400)	(4>253)	75.2	0	0	250

```
          v160       v170       v180       v190       v200       v210       v220
KRMDCPALPPGWKKEEVIRKSGLSAGKSDVYYFSPSGKKFRSKPQLARYLGNAVDLSSFDFRTGKMMPSK
KR :CPALP.GW.:EEV R:SGLSAG..DV:Y:SPSGKKFRSKPQLARYLG.::DLS:FDFRTGKM: :K
KRWECPALPQGWEREEVPRRSGLSAGHRDVFYYSPSGKKFRSKPQLARYLGGSMDLSTFDFRTGKMLMNK
      ^10        ^20        ^30        ^40        ^50        ^60        ^70

          v230       v240       v250       v260       v270       v280       v290
LQKNKQRLRNDPLNQNKGKPDLNITLPIRQTASIFKQPVTKFTNHPSNKVKSDPQRMNEQPRQLFWEKRL
::K::QR:R D: NQ KGKPDLNT:LP:RQTASIFKQPVTK:TNHPSNKVKSDPQ:  :QPRQLFWEK:L
MNKSRQRVRYDSSNQVKGKPDLNTALPVRQTASIFKQPVTKITNHPSNKVKSDPQKAVDQPRQLFWEKKL
      ^80        ^90        ^100       ^110       ^120       ^130       ^140
```

Fig 90

```
          v300       v310       v320       v330       v340       v350       v360
QGLSASDVTEQIIKIMELPKGLQGVGPGSNDETLLSAVASALHTSSAPITGQVSAAVEKNPAVWLNTSQP
 GLSA D::E::::TM:LPKGLQGVGPG..DETLLSA:ASALHTS: PITGQ:SAAVEKNP:VWLNT:QP
SGLSAFDIAEELVRTMDLPKGLQGVGPGCTDETLLSAIASALHTSTLPITGQLSAAVEKNPGVWLNTAQP
      ^150       ^160       ^170       ^180       ^190       ^200       ^210

          v370       v380       v390       v400
LCKAFIVTDEDIRKQEERVQQVRKKLEEALMADILSRAAD
LCKAF:VTD:DIRKQEE VQQVRK:LEEALMAD:L::..:
LCKAFMVTDDDIRKQEELVQQVRKRLEEALMADMLAHVEE
      ^220       ^230       ^240       ^250
```

FIG - 9P



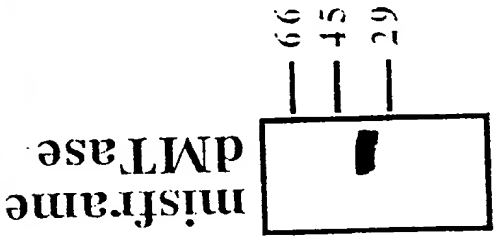


FIG - 10A

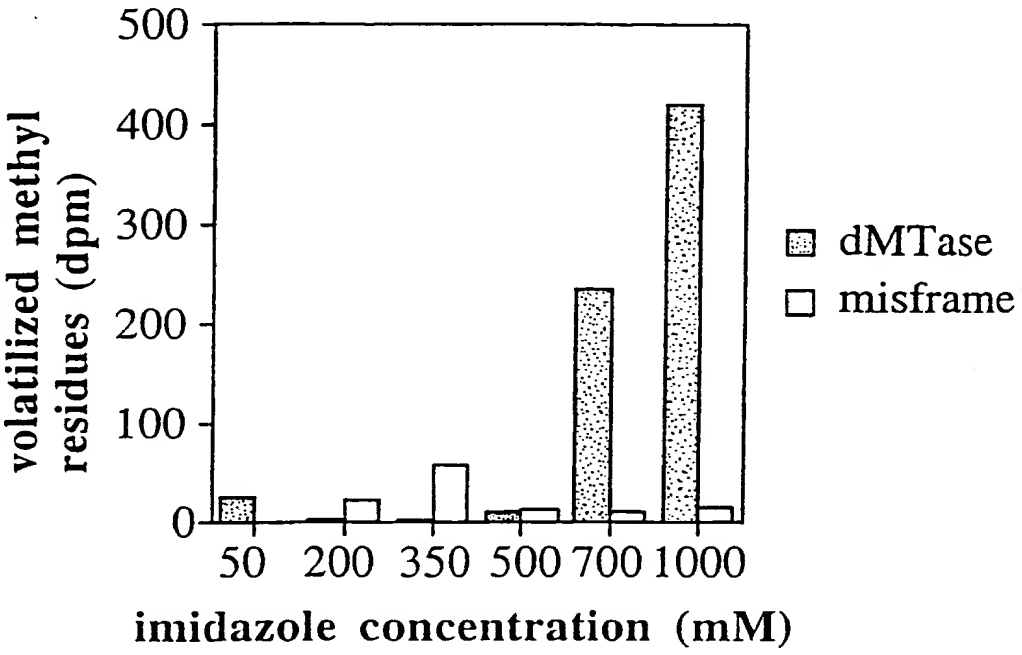

500
400
300
200
100
0
volatilized methyl residues (dpm)
50 200 350 500 700 1000
imidazole concentration (mM)
dMTase
misframe

Fig. 10B

volatilized methyl residues (dpm)
400
300
200
100
0
0 1 3 10 10+ Protease K
IMAC purified DNA dMTase (µl)
FIG. 10C
dMTase
misframe
—mdCMP
—dCMP
(mdCpdG)n
Time (min)
NM 0 15 30 60 120 180
FIG. 10D
mdCMP—
dCMP—
Substrate: pBluescript SK+

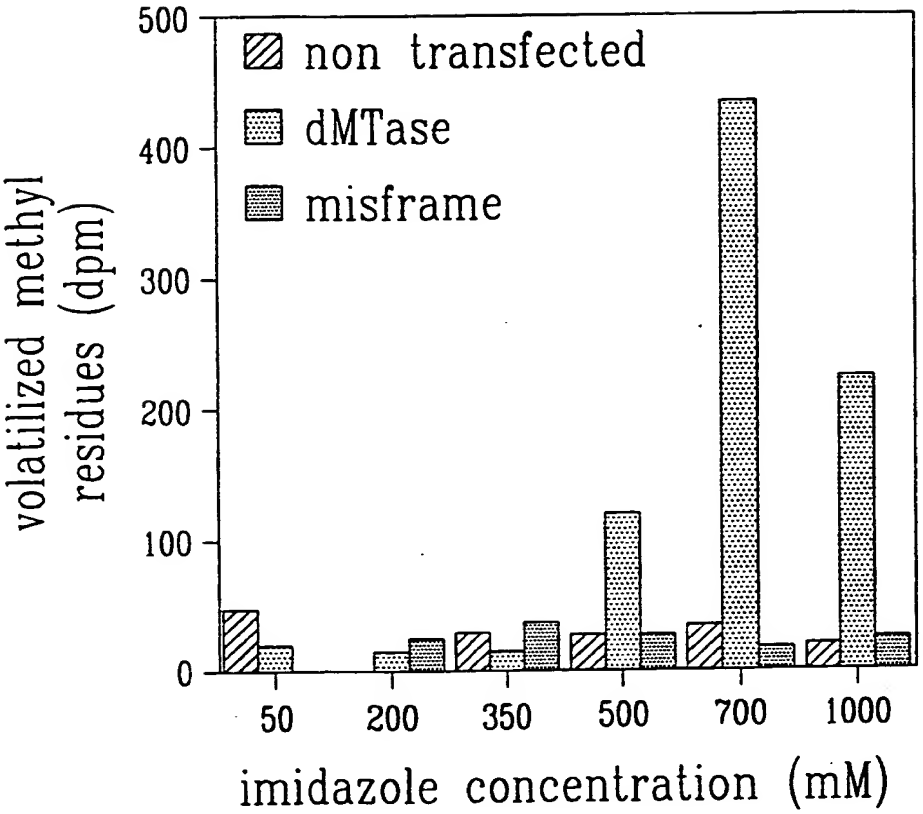

500
400
300
200
100
0
non transfected
dMTase
misframe
volatilized methyl residues (dpm)
50
200
350
500
700
1000
imidazole concentration (mM)

Fig. 11A

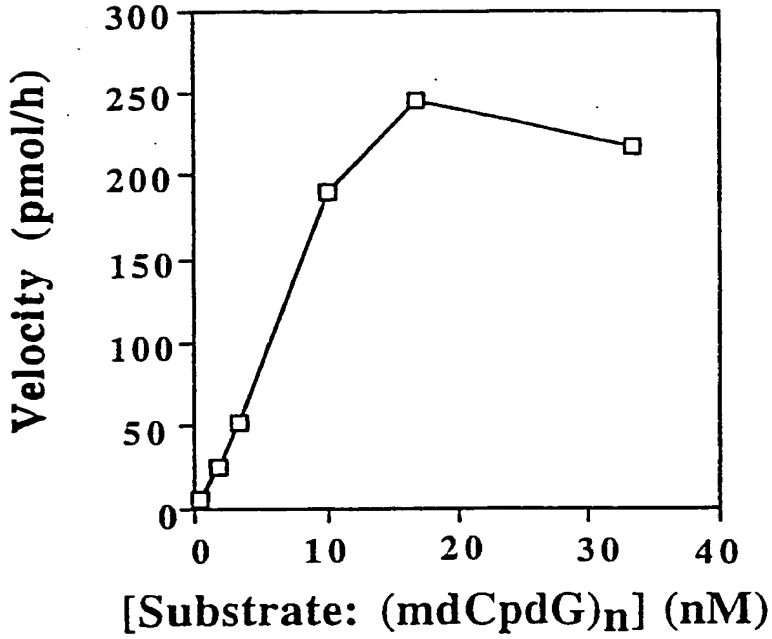
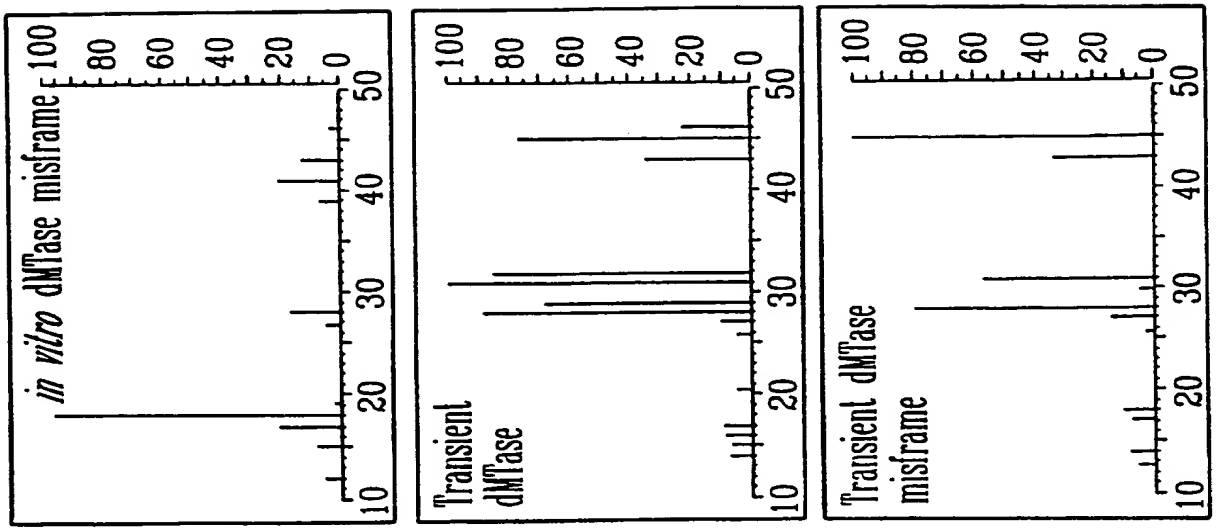

Velocity (pmol/h)
300
250
200
150
100
50
0
0
10
20
30
40
[Substrate: (mdCpdG)n] (nM)

Fig. 11F

FIG - 12A

Fig-12B


in vitro dMTase misframe
Transient dMTase
Transient dMTase misframe

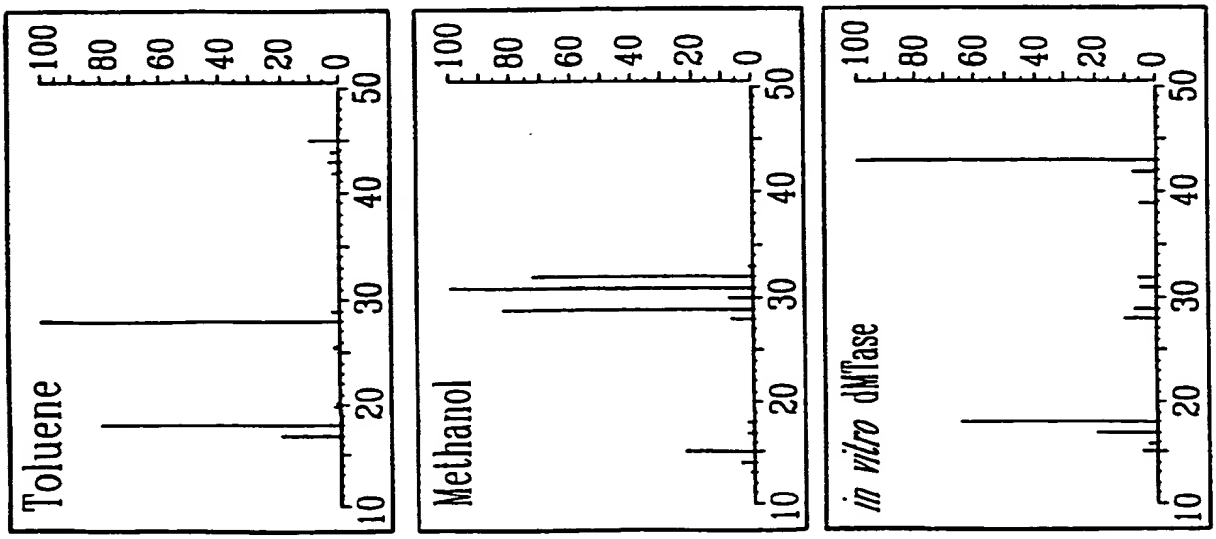

Toluene
Methanol
in vitro dMTase

Fig-13A

Fig-13B

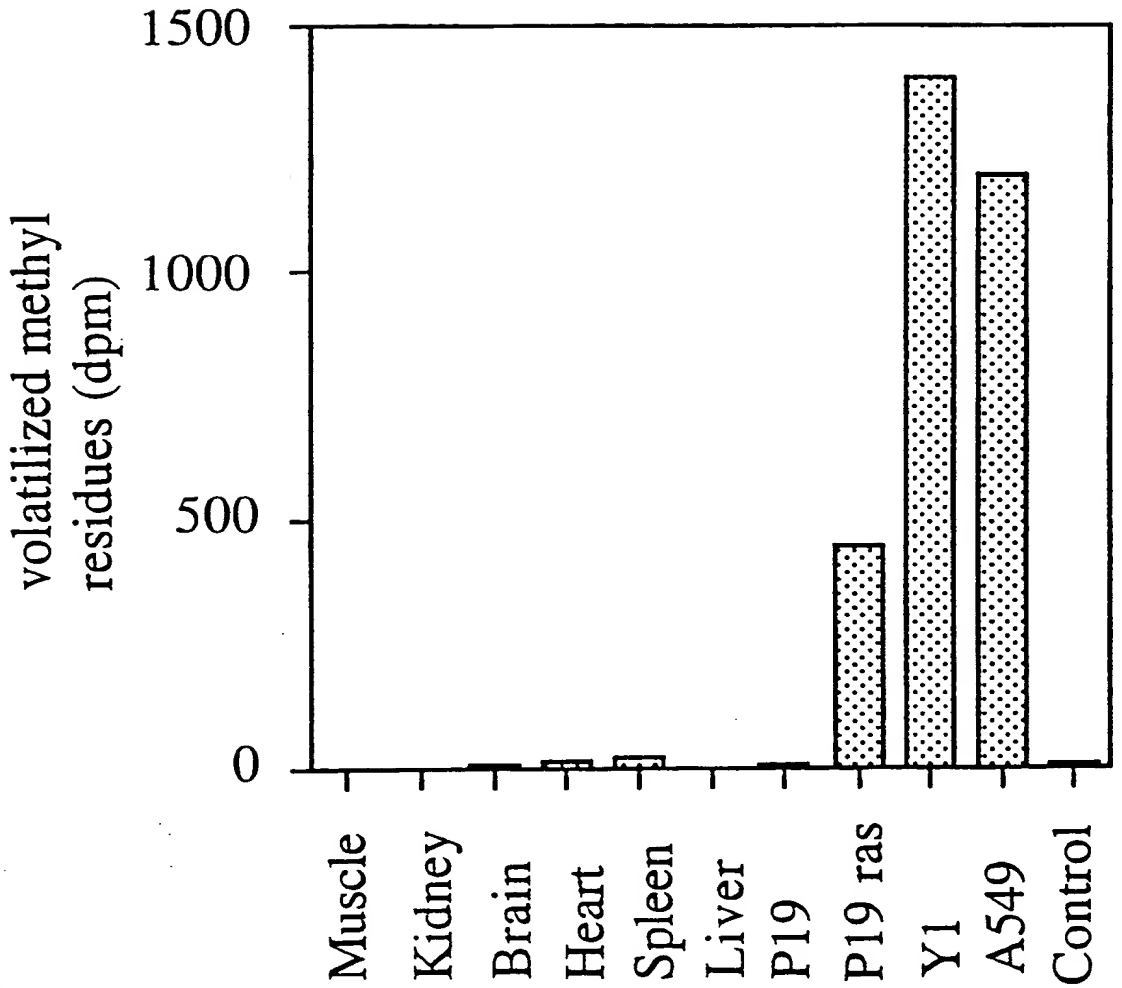
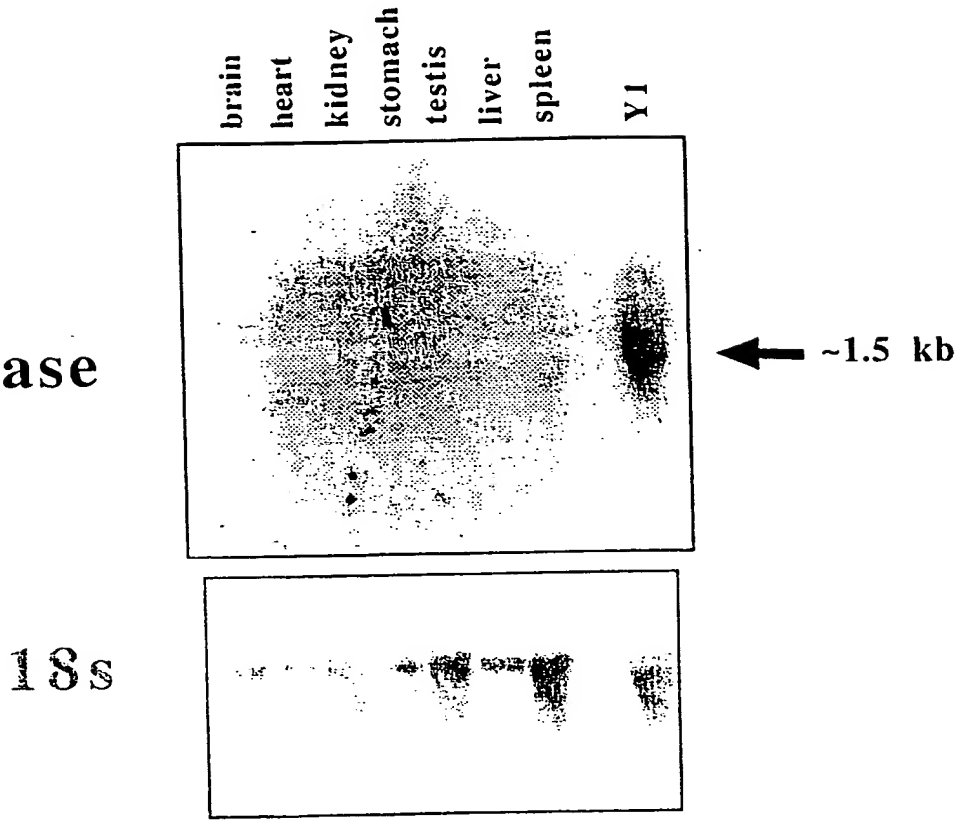

1500
1000
500
0
volatilized methyl residues (dpm)
Muscle
Kidney
Brain
Heart
Spleen
Liver
P19
P19 ras
Y1
A549
Control

FIG. 13C


brain
heart
kidney
stomach
testis
liver
spleen
Y1
dMTase
~1.5 kb
18s

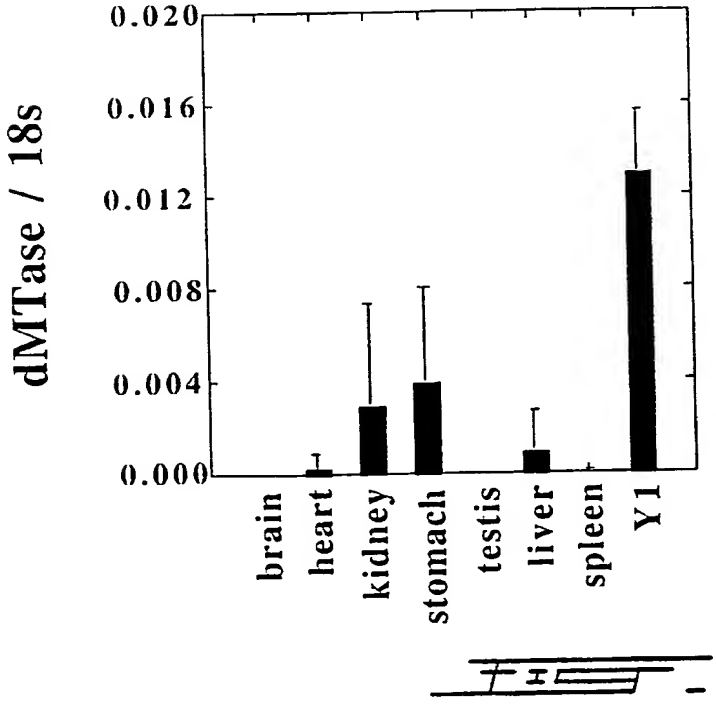

dMTase / 18s
0.020
0.016
0.012
0.008
0.004
0.000
brain
heart
kidney
stomach
testis
liver
spleen
Y1

FIG 13D

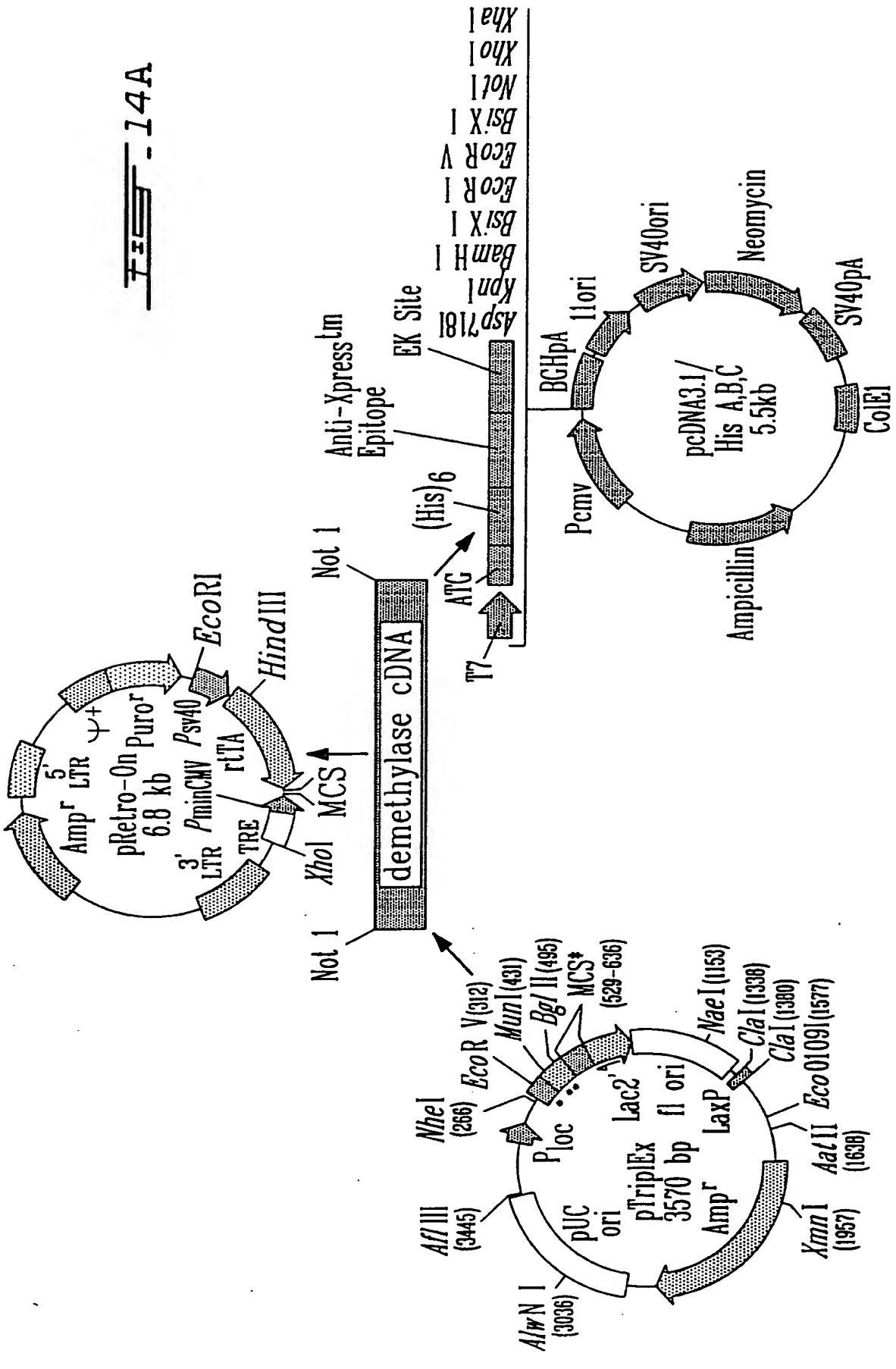

pRetro-On 6.8 kb
5' LTR
Ampr
ψ+
Puror
Psv40
PminCMV
rtTA
TRE
3' LTR
EcoRI
HindIII
XhoI MCS
Not 1
demethylase cDNA
Not 1
ATG
(His)6
Anti-Xpress tm Epitope
EK Site
T7
Asp718I
KpnI
BamH I
BsiX I
EcoR I
EcoR V
BsiX I
NotI
XhoI
XhaI
BGHpA
pcDNA3.1/ His A,B,C 5.5kb
f1ori
SV40ori
Neomycin
SV40pA
ColE1
Pcmv
Ampicillin
pTriplEx 3570 bp
Ploc
Lac2'
f1 ori
LaxP
Ampr
pUC ori
NheI (266)
EcoR V(312)
MunI(431)
BglII(495)
MCS*
(529-636)
NaeI(1153)
ClaI(1338)
ClaI(1380)
Eco0109I(1577)
AatII (1638)
XmnI (1957)
AflIII (3445)
AlwN I (3036)

FIG - 14A

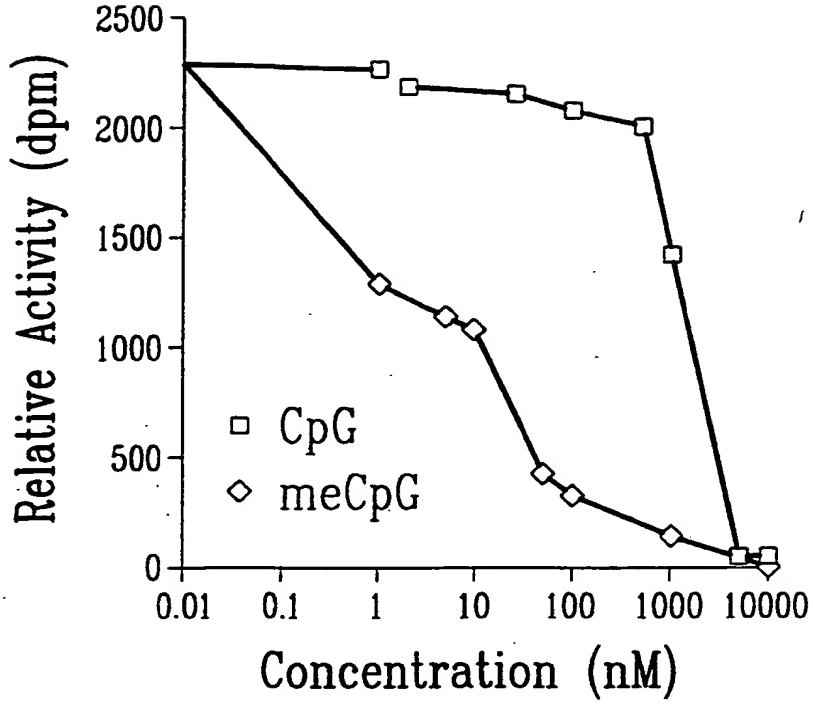


Fig. 14B

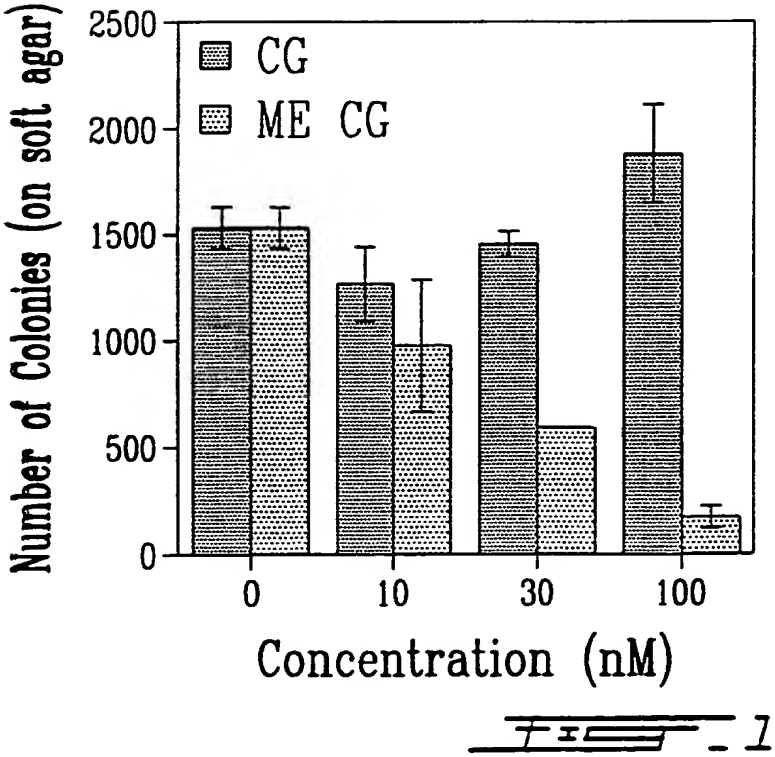
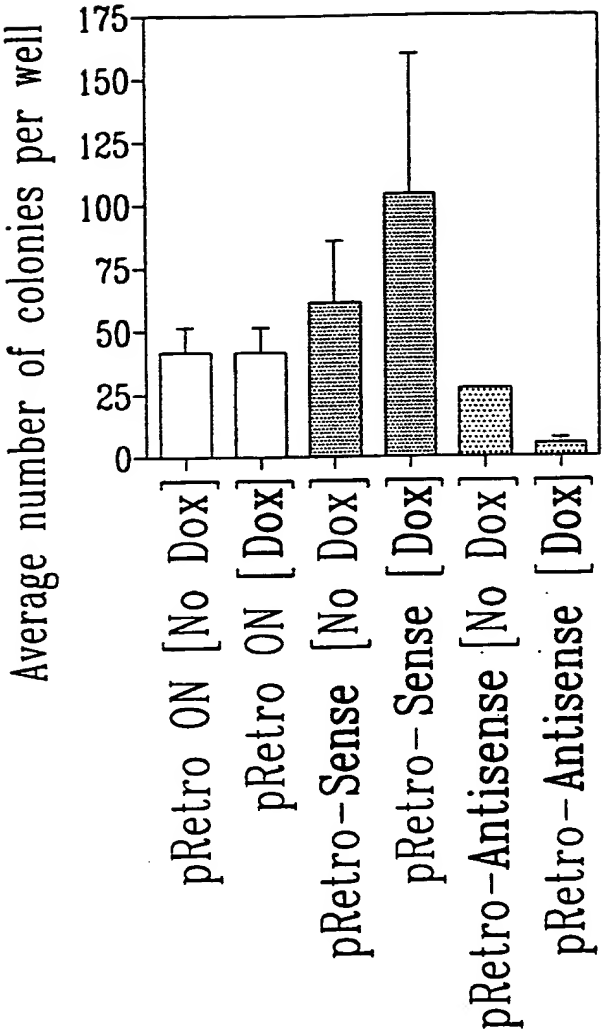


Fig. 14C


Average number of colonies per well
175
150
125
100
75
50
25
0
pRetro ON [No Dox]
pRetro ON [Dox]
pRetro-Sense [No Dox]
pRetro-Sense [Dox]
pRetro-Antisense [No Dox]
pRetro-Antisense [Dox]

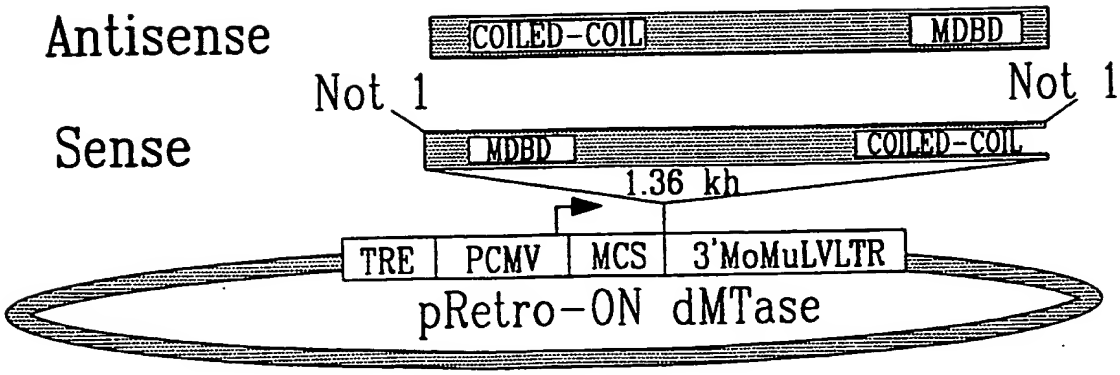

Antisense
Sense
COILED-COIL
MDBD
Not 1
Not 1
MDBD
COILED-COIL
1.36 kh
TRE
PCMV
MCS
3'MoMuLVLTR
pRetro-ON dMTase

Fig. 15

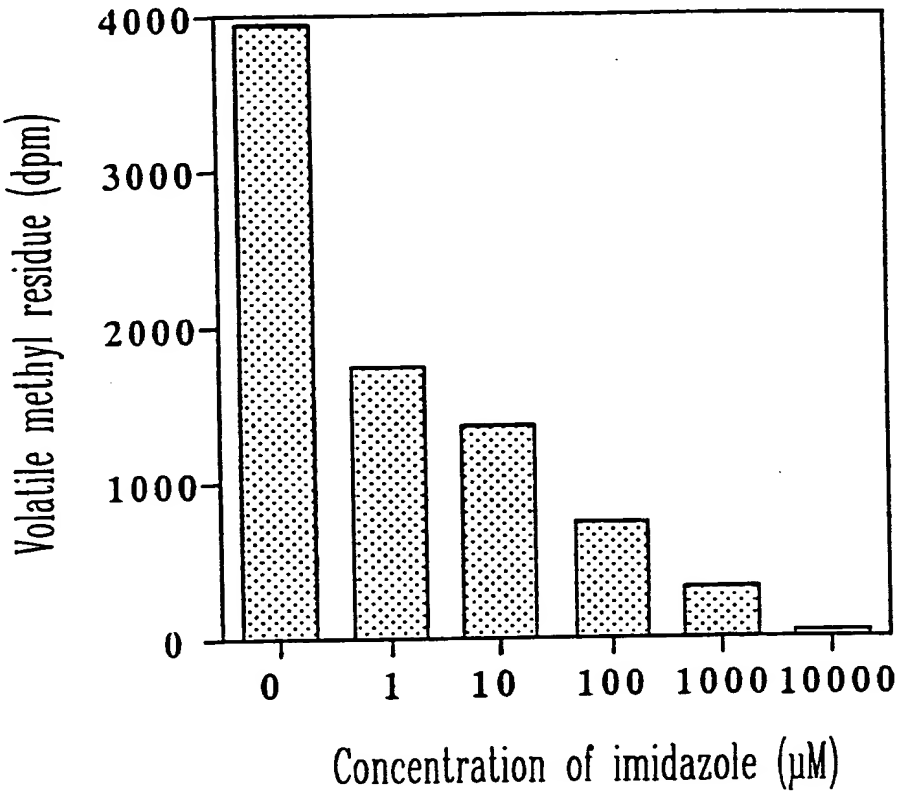

4000
3000
2000
1000
0
Volatile methyl residue (dpm)
0
1
10
100
1000
10000
Concentration of imidazole (μM)

Fig 16

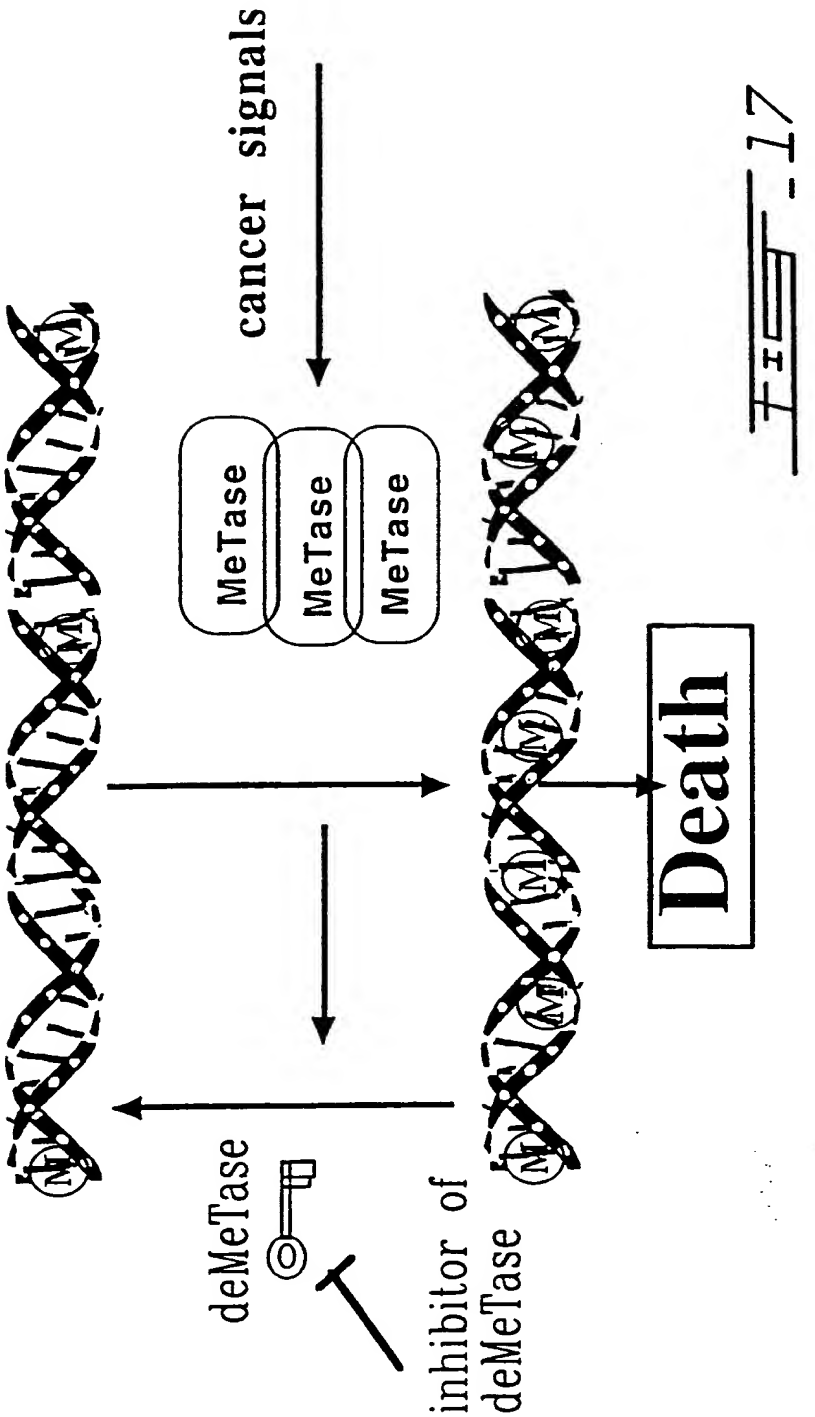


Fig - 17